Clinical Policy: Adalimumab (Humira), Adalimumab-afzb (Abrilada), Adalimumab-atto (Amjevita), Adalimumab-adbm (Cyltezo), Adalimumab-bwwd (Hadlima), Adalimumab-fkjp (Hulio), Adalimumab-adaz (Hyrimoz)

Reference Number: ERX.SPA.166
Effective Date: 10.01.16
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Lines of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Adalimumab (Humira®), adalimumab-afzb (Abrilada™), adalimumab-atto (Amjevita™), adalimumab-adbm (Cyltezo™), adalimumab-bwwd (Hadlima™), adalimumab-fkjp (Hulio®), and adalimumab-adaz (Hyrimoz™) are tumor necrosis factor (TNF) blockers.

FDA Approved Indication(s)

Indications	Description	Humira	Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz
Rheumatoid arthritis (RA)	Reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active RA	X	X
Juvenile idiopathic arthritis (JIA)	Reducing signs and symptoms of moderately to severely active polyarticular JIA in patients 2 years of age and older	X	X
Psoriatic arthritis (PsA)	Reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA	X	X
Ankylosing spondylitis (AS)	Reducing signs and symptoms in adult patients with active AS	X	X
Crohn's disease (CD)	Treatment of moderately to severely active CD in adults and pediatric patients 6 years of age and older	X	X
Adult ulcerative colitis (UC)	Treatment of moderately to severely active ulcerative colitis in adult patients Limitation of use: Effectiveness has not been established in patients who have lost response to or were intolerant to TNF blockers	X	X
Pediatric UC	Treatment of moderately to severely active UC in pediatric patients 5 years of age and older Limitation of use: Effectiveness has not been established in patients who have lost response to or were intolerant to TNF blockers	X	–
Plaque psoriasis (PsO)	Treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate	X	X
Hidradenitis suppurativa (HS)	Treatment of moderate to severe hidradenitis suppurativa in patients 12 years of age and older	X	–

Indications	Description	Humira	Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz
Uveitis (UV)	Treatment of non-infectious intermediate, posterior and panuveitis in adults and pediatric patients 2 years of age and older	X	–

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Humira, Abrilada, Amjevita, Cyltezo, Hadlima, Hulio, and Hyrimoz are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Ankylosing Spondylitis (must meet all)**:**
1. Diagnosis of AS;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Failure of at least TWO non-steroidal anti-inflammatory drugs (NSAIDs) at up to maximally indicated doses, each used for ≥ 4 weeks unless clinically significant adverse effects are experienced or all are contraindicated;
5. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
6. Dose does not exceed 40 mg every other week.

Approval duration: 6 months

B. Crohn's Disease (must meet all)**:**
1. Diagnosis of CD;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 6 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of at least ONE immunomodulator (e.g., azathioprine, 6-mercaptopurine [6-MP], methotrexate [MTX]) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
   b. Medical justification supports inability to use immunomodulators (*see Appendix E*);
5. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
6. Dose does not exceed one of the following (a or b):
   a. Adults: 160 mg on Day 1 and 80 mg on Day 15, followed by maintenance dose of 40 mg every other week starting Day 29;
   b. Pediatrics (i or ii):
      i. Weight 17 kg (37 lbs) to < 40 kg (88 lbs.): 80 mg on Day 1 and 40 mg on Day 15, followed by maintenance dose of 20 mg every other week starting Day 29;

ii. Weight ≥ 40 kg (88 lbs): 160 mg on Day 1 and 80 mg on Day 15, followed by maintenance dose of 40 mg every other week starting Day 29.

Approval duration: 6 months

C. Hidradenitis Suppurativa (must meet all)**:**
1. Diagnosis of HS;
2. Prescribed by a dermatologist, rheumatologist, or gastroenterologist;
3. Age ≥ 12 years;
4. Documentation of Hurley stage II or stage III (*see Appendix D*);
5. Failure of a ≥ 3 consecutive month trial of TWO of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated:
   a. Systemic antibiotic therapy (e.g., clindamycin, minocycline, doxycycline, rifampin);
   b. Oral retinoids;
   c. Hormonal treatment;
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. Dose does not exceed 160 mg on Day 1 and 80 mg on Day 15, followed by maintenance dose of 40 mg every week starting Day 29.

Approval duration: 6 months

D. Plaque Psoriasis (must meet all)**:**
1. Diagnosis of moderate-to-severe PsO as evidenced by involvement of one of the following (a or b):
   a. ≥ 3% of total body surface area;
   b. Hands, feet, scalp, face, or genital area;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX *(see Appendix D)*, and failure of a ≥ 3 consecutive month trial of cyclosporine or acitretin at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
5. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
6. Dose does not exceed 80 mg initial dose, followed by maintenance dose of 40 mg every other week starting one week after initial dose.

Approval duration: 6 months

E. Polyarticular Juvenile Idiopathic Arthritis (must meet all)**:**
1. Diagnosis of PJIA as evidenced by ≥ 5 joints with active arthritis;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 2 years;
4. Documented baseline 10-joint clinical juvenile arthritis disease activity score (cJADAS-10) (*see Appendix J*);
5. Member meets one of the following (a, b, c, or d):
   a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of leflunomide or sulfasalazine at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated;
   c. For sacroiliitis/axial spine involvement (i.e., spine, hip), failure of a ≥ 4 week trial of an NSAID at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;

d. Documented presence of high disease activity as evidenced by a cJADAS-10 > 8.5 (*see Appendix J*);

6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. Dose does not exceed one of the following (a, b, or c):
   a. Weight 10 kg (22 lbs) to <15 kg (33 lbs): 10 mg every other week;
   b. Weight 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg every other week;
   c. Weight ≥ 30 kg (66 lbs): 40 mg every other week.

Approval duration: 6 months

F. Psoriatic Arthritis (must meet all)**:**

1. Diagnosis of PsA;
2. Prescribed by or in consultation with a dermatologist or rheumatologist;
3. Age ≥ 18 years;
4. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
5. Dose does not exceed 40 mg every other week.

Approval duration: 6 months

G. Rheumatoid Arthritis (must meet all)**:**

1. Diagnosis of RA per American College of Rheumatology (ACR) criteria (*see Appendix G*);
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 18 years;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 3 consecutive month trial of MTX at up to maximally indicated doses;
   b. Member has intolerance or contraindication to MTX (*see Appendix D*), and failure of a ≥ 3 consecutive month trial of at least ONE conventional disease-modifying antirheumatic drug [DMARD] (e.g., sulfasalazine, leflunomide, hydroxychloroquine) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
5. Documentation of one of the following baseline assessment scores (a or b):
   a. Clinical disease activity index (CDAI) score (*see Appendix H*);
   b. Routine assessment of patient index data 3 (RAPID) score (*see Appendix I*);
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. Dose does not exceed one of the following (a or b):
   a. 40 mg every other week;
   b. 40 mg every week and one of the following (i and ii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of 40 mg every other week;
      ii. Member is not a candidate for concurrent methotrexate and Humira due to contraindications or intolerance.

Approval duration: 6 months

H. Ulcerative Colitis (must meet all)**:**

1. Diagnosis of UC;
2. Prescribed by or in consultation with a gastroenterologist;
3. Age ≥ 5 years;
4. Documentation of a Mayo Score ≥ 6 (*see Appendix F*);
5. Failure of an 8-week trial of systemic corticosteroids, unless contraindicated or clinically significant adverse effects are experienced;

6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
7. Dose does not exceed one of the following (a, b, or c):
   a. 160 mg on Day 1 and 80 mg on Day 15, followed by maintenance dose of 40 mg every other week starting Day 29;
   b. For pediatric patients weighing more than 20 kg, but less than 40 kg: 80 mg on Day 1, 40 mg on Day 8 and Day 15, followed by maintenance doses of 40 mg every other week or 20 mg every week;
   c. For pediatric patients weighing more than 40 kg: 160 mg on Day 1 and 80 mg on Day 8 and 15, followed by maintenance doses of 80 mg every other week or 40 mg every week.

Approval duration: 6 months

I. Uveitis (must meet all):
1. Diagnosis of non-infectious intermediate, posterior, or panuveitis;
2. Prescribed by or in consultation with an ophthalmologist or rheumatologist;
3. Age ≥ 2 years;
4. Failure of a ≥ 2 week trial of a systemic corticosteroid (e.g., prednisone) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
5. Failure of a trial of a non-biologic immunosuppressive therapy (e.g., azathioprine, MTX, mycophenolate mofetil, cyclosporine, tacrolimus, cyclophosphamide, chlorambucil) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated;
6. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (see Section III: Diagnoses/Indications for which coverage is NOT authorized);
7. Dose does not exceed 80 mg initial dose, followed by maintenance dose of 40 mg every other week starting one week after initial dose.

J. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Rheumatoid Arthritis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a or b):
   a. A decrease in CDAI (*see Appendix H*) or RAPID3 (*see Appendix I*) score from baseline;
   b. Medical justification stating ability to conduct CDAI re-assessment, and submission of RAPID3 score associated with disease severity that is similar to initial CDAI assessment or improved;
3. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
4. If request is for a dose increase, new dose does not exceed one of the following (a or b):*
   a. 40 mg every other week;
   b. 40 mg every week and one of the following (i or ii):
      i. Documentation supports inadequate response to a ≥ 3 month trial of 40 mg every other week;
      ii. Member is not a candidate for concurrent methotrexate and Humira due to contraindications or intolerance.

Approval duration: 12 months*
**(If new dosing regimen, approve for 6 months)*

B. All Other Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member meets one of the following (a, b, or c):
   a. For HS: At least a 25% reduction in inflammatory nodules and abscesses;
   b. For pJIA: Member is responding positively to therapy as evidenced by a decrease in cJADAS-10 from baseline (*see Appendix J*);
   c. For all other indications: Member is responding positively to therapy;
3. Member does not have combination use with biological disease-modifying antirheumatic drugs or Janus kinase inhibitors (*see Section III: Diagnoses/Indications for which coverage is NOT authorized*);
4. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
   a. PJIA, PsA, AS, CD, PsO, UV: 40 mg every other week;
   b. HS: 40 mg every week;
   c. UC: one of the following (i or ii):
      i. 40 mg every other week or 20 mg every week;
      ii. 80 mg every other week or 40 mg every week, and member initiated Humira prior to 18 years of age.

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;

B. Combination use with biological disease-modifying antirheumatic drugs (bDMARDs) or potent immunosuppressants, including but not limited to any tumor necrosis factor (TNF) antagonists [e.g., Cimzia®, Enbrel®, Humira®, Simponi®, Avsola™, Inflectra™, Remicade®, Renflexis™], interleukin agents [e.g., Arcalyst® (IL-1 blocker), Ilaris® (IL-1 blocker), Kineret® (IL-1RA), Actemra® (IL-6RA), Kevzara® (IL-6RA), Stelara® (IL-12/23 inhibitor), Cosentyx® (IL-17A inhibitor), Taltz® (IL-17A inhibitor), Siliq™ (IL-17RA), Ilumya™ (IL-23 inhibitor), Skyrizi™ (IL-23 inhibitor), Tremfya® (IL-23 inhibitor)], Janus kinase inhibitors (JAKi) [e.g., Xeljanz®/Xeljanz® XR, Cibinqo™, Olumiant™, Rinvoq™], anti-CD20 monoclonal antibodies [Rituxan®, Riabni™, Ruxience™, Truxima®, Rituxan Hycela®], selective co-stimulation modulators [Orencia®], and integrin receptor antagonists [Entyvio®] because of the additive immunosuppression, increased risk of neutropenia, as well as increased risk of serious infections.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

6-MP: 6-mercaptopurine
AS: ankylosing spondylitis
CD: Crohn's disease
CDAI: clinical disease activity index
cJADAS: clinical juvenile arthritis disease activity score
DMARD: disease-modifying antirheumatic drug
FDA: Food and Drug Administration
GI: gastrointestinal
HS: hidradenitis suppurative
JAKi: Janus kinase inhibitors
MTX: methotrexate
NSAIDs: nonsteroidal anti-inflammatory drugs
PJIA: polyarticular juvenile idiopathic arthritis
PsA: psoriatic arthritis
PsO: psoriasis
RA: rheumatoid arthritis
RAPID3: routine assessment of patient index data 3
TNF: tumor necrosis factor
UC: ulcerative colitis
UV: uveitis

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
acitretin (Soriatane®)	**PsO** 25 or 50 mg PO QD	50 mg/day
azathioprine (Azasan®, Imuran®)	**RA** 1 mg/kg/day PO QD or divided BID **CD*, UV*** 1.5 – 2 mg/kg/day PO	2.5 mg/kg/day
chlorambucil (Leukeran®)	**UV*** 0.2 mg/kg PO QD, then taper to 0.1 mg/kg PO QD or less	0.2 mg/kg/day
clindamycin (Cleocin®) + rifampin (Rifadin®)	**HS*** clindamycin 300 mg PO BID and rifampin 300 mg PO BID	clindamycin: 1,800 mg/day rifampin: 600 mg/day
corticosteroids	**CD*** prednisone 40 mg PO QD for 2 weeks or IV 50 – 100 mg Q6H for 1 week budesonide (Entocort EC®) 6 – 9 mg PO QD **UV*** prednisone 5 – 60 mg/day PO in 1 – 4 divided doses	Various
Cuprimine® (d-penicillamine)	**RA*** <u>Initial dose:</u> 125 or 250 mg PO QD <u>Maintenance dose:</u> 500 – 750 mg/day PO QD	1,500 mg/day
cyclophosphamide (Cytoxan®)	**UV*** 1 – 2 mg/kg/day PO	N/A
cyclosporine (Sandimmune®, Neoral®)	**PsO** 2.5 mg/kg/day PO divided BID **RA** 2.5 – 4 mg/kg/day PO divided BID **UV*** 2.5 – 5 mg/kg/day PO in divided doses	PsO, RA: 4 mg/kg/day UV: 5 mg/kg/day
doxycycline (Acticlate®)	**HS*** 50 – 100 mg PO BID	300 mg/day
hormonal agents (e.g., estrogen-containing combined oral contraceptives, spironolactone)	**HS** varies	varies
hydroxychloroquine (Plaquenil®)	**RA*** <u>Initial dose:</u> 400 – 600 mg/day PO QD	600 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Maintenance dose: 200 – 400 mg/day PO QD	
isotretinoin (Absorica®, Amnesteem®, Claravis®, Myorisan®, Zenatane®)	**HS** varies	varies 1.6 to 2 mg/kg/day
leflunomide (Arava®)	**PJIA*** Weight < 20 kg: 10 mg every other day PO Weight 20 - 40 kg: 10 mg/day PO Weight > 40 kg: 20 mg/day PO **RA** 100 mg PO QD for 3 days, then 20 mg PO QD	20 mg/day
6-mercaptopurine (Purixan®)	**CD*, UC*** 50 mg PO QD or 1 – 2 mg/kg/day PO	2 mg/kg/day
methotrexate (Rheumatrex®)	**CD*** 15 – 25 mg/week IM or SC **PsO** 10 – 25 mg/week PO or 2.5 mg PO Q12 hr for 3 doses/week **PJIA*** 10 – 20 mg/m^2/week PO, SC, or IM **RA** 7.5 mg/week PO, SC, or IM or 2.5 mg PO Q12 hr for 3 doses/week **UV*** 7.5 – 20 mg/week PO	30 mg/week
minocycline (Minocin®)	**HS** 50 – 100 mg PO BID	200 mg/day
mycophenolate mofetil (Cellcept®)	**UV*** 500 – 1,000 mg PO BID	3 g/day
NSAIDs (e.g., indomethacin, ibuprofen, naproxen, celecoxib)	**AS** Varies	Varies
Pentasa® (mesalamine)	**CD** 1,000 mg PO QID	4 g/day
Ridaura® (auranofin)	**RA** 6 mg PO QD or 3 mg PO BID	9 mg/day (3 mg TID)
sulfasalazine (Azulfidine®)	**PJIA*** 30-50 mg/kg/day PO divided BID **RA** 2 g/day PO in divided doses	PJIA: 2 g/day RA: 3 g/day
tacrolimus (Prograf®)	**CD** 0.27 mg/kg/day PO in divided doses or 0.15 – 0.29 mg/kg/day PO	N/A

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	UV 0.1-0.15 mg/kg/day PO	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
**Off-label*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s):
  - Serious infections
  - Malignancy

Appendix D: General Information

- Definition of failure of MTX or DMARDs:
  - Child-bearing age is not considered a contraindication for use of MTX. Each drug has risks in pregnancy. An educated patient and family planning would allow use of MTX in patients who have no intention of immediate pregnancy.
  - Social use of alcohol is not considered a contraindication for use of MTX. MTX may only be contraindicated if patients choose to drink over 14 units of alcohol per week. However, excessive alcohol drinking can lead to worsening of the condition, so patients who are serious about clinical response to therapy should refrain from excessive alcohol consumption.
- Examples of positive response to therapy may include, but are not limited to:
  - Reduction in joint pain/swelling/tenderness
  - Improvement in ESR/CRP levels
  - Improvements in activities of daily living
- Hidradenitis suppurativa:
  - HS is sometimes referred to as: "acne inversa, acne conglobata, apocrine acne, apocrinitis, Fox-den disease, hidradenitis axillaris, HS, pyodermia sinifica fistulans, Velpeau's disease, and Verneuil's disease."
  - In HS, Hurley stages are used to determine severity of disease. Hurley stage II indicates moderate disease, and is characterized by recurrent abscesses, with sinus tracts and scarring, presenting as single or multiple widely separated lesions. Hurley stage III indicates severe disease, and is characterized by diffuse or near-diffuse involvement presenting as multiple interconnected tracts and abscesses across an entire area.
- Ulcerative colitis: there is insufficient evidence to support the off-label weekly dosing of Humira for the treatment of moderate-to-severe UC. It is the position of Envolve Pharmacy Solutions that the off-label weekly dosing of Humira for the treatment of moderate-to-severe UC is investigational and not medically necessary at this time.
  - The evidence from the *post hoc* study of the Humira pivotal trial suggests further studies are needed to confirm the benefit of weekly Humira dosing for the treatment of UC in patients with inadequate or loss of therapeutic response to treatment with Humira every other week. No large, randomized or prospective studies have been published to support the efficacy of the higher frequency of dosing, while national and international treatment guidelines also do not strongly support dose escalation of Humira for UC. The current market consensus is that weekly dosing of Humira is not medically necessary due to lack of evidence to support its benefit.

Appendix E: Immunomodulator Medical Justification

- The following may be considered for medical justification supporting inability to use an immunomodulator for Crohn's disease:
  - Inability to induce short-term symptomatic remission with a 3-month trial of systemic glucocorticoids
  - High-risk factors for intestinal complications may include:

- Initial extensive ileal, ileocolonic, or proximal GI involvement
- Initial extensive perianal/severe rectal disease
- Fistulizing disease (e.g., perianal, enterocutaneous, and rectovaginal fistulas)
- Deep ulcerations
- Penetrating, stricturing or stenosis disease and/or phenotype
- Intestinal obstruction or abscess

- High risk factors for postoperative recurrence may include:
  - Less than 10 years duration between time of diagnosis and surgery
  - Disease location in the ileum and colon
  - Perianal fistula
  - Prior history of surgical resection
  - Use of corticosteroids prior to surgery

Appendix F: Mayo Score

- Mayo Score: evaluates ulcerative colitis stage, based on four parameters: stool frequency, rectal bleeding, endoscopic evaluation and Physician's global assessment. Each parameter of the score ranges from zero (normal or inactive disease) to 3 (severe activity) with an overall score of 12.

Score	Decoding
0 – 2	Remission
3 – 5	Mild activity
6 – 10	Moderate activity
>10	Severe activity

Appendix G: The 2010 ACR Classification Criteria for RA

Add score of categories A through D; a score of ≥ 6 out of 10 is needed for classification of a patient as having definite RA.

A	**Joint involvement**	Score
	1 large joint	0
	2-10 large joints	1
	1-3 small joints (with or without involvement of large joints)	2
	4-10 small joints (with or without involvement of large joints)	3
	> 10 joints (at least one small joint)	5
B	**Serology (at least one test result is needed for classification)**	
	Negative rheumatoid factor (RF) *and* negative anti-citrullinated protein antibody (ACPA)	0
	Low positive RF *or* low positive ACPA ** Low: < 3 x upper limit of normal*	2
	High positive RF *or* high positive ACPA ** High: ≥ 3 x upper limit of normal*	3
C	**Acute phase reactants (at least one test result is needed for classification)**	
	Normal C-reactive protein (CRP) and normal erythrocyte sedimentation rate (ESR)	0
	Abnormal CRP or abnormal ESR	1
D	**Duration of symptoms**	
	< 6 weeks	0
	≥ 6 weeks	1

Appendix H: Clinical Disease Activity Index (CDAI) Score

The Clinical Disease Activity Index (CDAI) is a composite index for assessing disease activity in RA. CDAI is based on the simple summation of the count of swollen/tender joint count of 28 joints along with patient and physician global assessment on VAS (0–10 cm) Scale for estimating disease activity. The CDAI score ranges from 0 to 76.

CDAI Score	Disease state interpretation
≤ 2.8	Remission
> 2.8 to ≤ 10	Low disease activity
> 10 to ≤ 22	Moderate disease activity

CDAI Score	Disease state interpretation
> 22	High disease activity

Appendix I: Routine Assessment of Patient Index Data 3 (RAPID3) Score
The Routine Assessment of Patient Index Data 3 (RAPID3) is a pooled index of the three patient-reported ACR core data set measures: function, pain, and patient global estimate of status. Each of the individual measures is scored 0 – 10, and the maximum achievable score is 30.

RAPID3 Score	Disease state interpretation
≤ 3	Remission
3.1 to 6	Low disease activity
6.1 to 12	Moderate disease activity
> 12	High disease activity

Appendix J: Clinical Juvenile Arthritis Disease Activity Score based on 10 joints (cJADAS-10)
The cJADAS10 is a continuous disease activity score specific to JIA and consisting of the following three parameters totaling a maximum of 30 points:

- Physician's global assessment of disease activity measured on a 0-10 visual analog scale (VAS), where 0 = no activity and 10 = maximum activity;
- Parent global assessment of well-being measured on a 0-10 VAS, where 0 = very well and 10 = very poor;
- Count of joints with active disease to a maximum count of 10 active joints*

**ACR definition of active joint: presence of swelling (not due to currently inactive synovitis or to bony enlargement) or, if swelling is not present, limitation of motion accompanied by pain, tenderness, or both*

cJADAS-10	Disease state interpretation
≤ 1	Inactive disease
1.1 to 2.5	Low disease activity
2.51 to 8.5	Moderate disease activity
> 8.5	High disease activity

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RA	40 mg SC every other week Some patients with RA not receiving concomitant methotrexate may benefit from increasing the frequency to 40 mg every week or 80 mg every other week.	40 mg/week
PJIA	Weight 10 kg (22 lbs) to <15 kg (33 lbs): 10 mg SC every other week Weight 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg SC every other week Weight ≥ 30 kg (66 lbs): 40 mg SC every other week	40 mg every other week
PsA AS	40 mg SC every other week	40 mg every other week
CD	Initial dose: *Adults:* 160 mg SC on Day 1, then 80 mg SC on Day 15 *Pediatrics:* Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 80 mg SC on Day 1, then 40 mg SC on Day 15 Weight ≥ 40 kg (88 lbs): 160 mg SC on Day 1, then 80 mg SC on Day 15 Maintenance dose: *Adults:* 40 mg SC every other week starting on Day 29	40 mg every other week

<table>
<tr><th>Indication</th><th>Dosing Regimen</th><th>Maximum Dose</th></tr>
<tr><td></td><td>Pediatrics:
Weight 17 kg (37 lbs) to < 40 kg (88 lbs): 20 mg SC every other week starting on Day 29
Weight ≥ 40 kg (88 lbs): 40 mg SC every other week starting on Day 29</td><td></td></tr>
<tr><td>UC</td><td><u>Initial dose:</u>
Adults: 160 mg SC on Day 1, then 80 mg SC on Day 15

Pediatrics:
<table>
<tr><th>Weight</th><th>Days 1 through 15</th></tr>
<tr><td>20 kg to less than 40 kg</td><td>Day 1: 80 mg
Day 8: 40 mg
Day 15: 40 mg</td></tr>
<tr><td>40 kg and greater</td><td>Day 1: 160 mg (single dose or split over two consecutive days)
Day 8: 80 mg
Day 15: 80 mg</td></tr>
</table>
<u>Maintenance dose:</u>
Adults: 40 mg SC every other week starting on Day 29

Pediatrics:
<table>
<tr><th>Weight</th><th>Starting on Day 29*</th></tr>
<tr><td>20 kg to less than 40 kg</td><td>40 mg every other week or 20 mg every week</td></tr>
<tr><td>40 kg and greater</td><td>80 mg every other week or 40 mg every week</td></tr>
</table>
*Continue the recommended pediatric dosage in patients who turn 18 years of age and who are well-controlled on Humira regimen.</td><td>40 mg every other week</td></tr>
<tr><td>PsO</td><td><u>Initial dose:</u>
80 mg SC
<u>Maintenance dose:</u>
40 mg SC every other week starting one week after initial dose</td><td>40 mg every other week</td></tr>
<tr><td>UV</td><td>Pediatrics:
Weight 10 kg (22 lbs) to < 15 kg (33 lbs): 10 mg SC every other week
Weight 15 kg (33 lbs) to < 30 kg (66 lbs): 20 mg SC every other week
Weight ≥ 30 kg (66 lbs): 40 mg SC every other week

Adults:
Initial dose of 80 mg SC, followed by 40 mg SC every other week starting one week after the initial dose</td><td>40 mg every other week</td></tr>
<tr><td>HS</td><td>For patients 12 years of age and older weighing at least 30 kg:
<u>Initial dose:</u>
Weight 30 kg (66 lbS) to < 60 kg (132 lbs): 80 mg SC on Day 1, then 40 mg on Day 8
Weight ≥ 60 kg (132 lbs): 160 mg SC on Day 1, then 80 mg SC on Day 15

<u>Maintenance dose:</u>
Weight 30 kg (66 lbS) to < 60 kg (132 lbs): 40 mg every other week
Weight ≥ 60 kg (132 lbs): 40 mg SC once weekly starting on Day 29</td><td>40 mg/week</td></tr>
</table>

VI. Product Availability

Drug Name	Availability
Adalimumab (Humira)	• Single-dose prefilled pen: 80 mg/0.8 mL, 40 mg/0.8 mL, 40 mg/0.4 mL • Single-dose prefilled syringe: 80 mg/0.8 mL, 40 mg/0.8 mL, 40 mg/0.4 mL, 20 mg/0.4 mL, 20 mg/0.2 mL, 10 mg/0.2 mL, 10 mg/0.1 mL • Single-use vial for institutional use only: 40 mg/0.8 mL
Adalimumab-afzb (Abrilada)	• Single-dose prefilled pen (Abrilada Pen): 40 mg/0.8 mL • Single dose prefilled syringe: 40 mg/0.8 mL, 20 mg/0.4 mL, 10 mg/0.2 mL • Single-dose glass vial for institutional use only: 40 mg/0.8 mL
Adalimumab-atto (Amjevita)	• Single-dose prefilled SureClick autoinjector: 40 mg/0.8 mL • Single-dose prefilled syringe: 40 mg/0.8 mL, 20 mg/0.4 mL
Adalimumab-adbm (Cyltezo)	• Single-dose prefilled syringe: 40 mg/0.8 mL, 20 mg/0.4 mL
Adalimumab-bwwd (Hadlima)	• Single-dose prefilled autoinjector (Hadlima PushTouch): 40 mg/0.8 mL, 40 mg/0.4 mL (citrate-free) • Single-dose prefilled syringe: 40 mg/0.8 mL, 40 mg/0.4 mL (citrate-free) • Single-dose glass vial for institutional use only: 40 mg/.8mL
Adalimumab-fkjp (Hulio)	• Single-dose prefilled pen (Hulio Pen): 40 mg/0.8 mL • Single-dose prefilled syringe: 40 mg/0.8 mL, 20 mg/0.4 mL
Adalimumab-adaz (Hyrimoz)	• Single-dose prefilled glass syringe (with BD UltraSafe Passive™ Needle Guard): 40 mg/0.8 mL • Single-dose prefilled pen (Sensoready® Pen): 40 mg/0.8 mL • Single-dose prefilled glass syringe: 10 mg/0.2 mL

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2018 annual review: removed disease qualifiers (i.e., moderate-to-severe); modified trial and failure for RA to at least one conventional DMARD; modified gastroenterologist specialty requirement to gastrointestinal specialist for CD/UC; added age-specific max dosing requirement for CD; added aminosalicylate as an option for trial and failure for UC; generalized trial of failure of systemic antibiotics for HS modified trial and failure for UV to require	02.27.18	05.18

Reviews, Revisions, and Approvals	Date	P&T Approval Date
both systemic corticosteroid and immunosuppressive therapy; references reviewed and updated.		
4Q 2018 annual review: updated pediatric indication expansion for uveitis and adolescent indication expansion for hidradenitis suppurativa; modified prescriber specialist from GI specialist to gastroenterologist for CD, UC, and HS; added trial and failure of immunosuppressants, or medical necessity for use of biologics in CD; allowed bypassing conventional DMARDs for axial PsA and required trial of NSAIDs; references reviewed and updated.	08.28.18	11.18
2Q 2019 annual review: removed trial and failure of conventional DMARDs (e.g., MTX)/NSAIDs for PsA per 2018 ACR/NPF guidelines; revised approval duration to 6 months if request is for continuation of therapy with a new (e.g, increased dose/frequency) regimen; references reviewed and updated.	03.05.19	05.19
RT4: no significant change; added biosimilar Amjevita to policy.	06.18.19	
RT4: no significant change; added biosimilars Cyltezo and Hadlima to policy.	09.23.19	
2Q 2020 annual review: added Hyrimoz to the policy; for UC, revised redirection from AZA, 6-MP, and ASA to corticosteroids and added requirement of Mayo score of at least 6; for RA, added specific diagnostic criteria for definite RA, baseline CDAI score requirement, and decrease in CDAI score as positive response to therapy; for HS, revised requirement from systemic antibiotics to additionally require oral retinoids or hormonal therapy, and required at least a 25% reduction in inflammatory nodules and abscesses for reauthorization; references reviewed and updated.	02.28.20	05.20
Revised typo in Appendix E from “normal ESR” to “abnormal ESR” for a point gained for ACR Classification Criteria.	11.22.20	
Updated pJIA criteria to require diagnosis as evidenced by ≥ 5 joints and cJADAS assessment. Additionally, updated criteria to allow tiered redirection or bypass of MTX in the event of sacroiliitis or high disease activity. Added criteria for RAPID3 assessment for RA given limited in-person visits during COVID-19 pandemic, updated appendices.	11.24.20	02.21
2Q 2021 annual review: added additional criteria related to diagnosis of moderate-to-severe PsO per 2019 AAD/NPF guidelines specifying at least 3% BSA involvement or involvement of areas that severely impact daily function; for RA: applied dose escalation language to initial authorization criteria and removed trial and failure requirements as Humira is preferred for 500/550; added combination of bDMARDs under Section III; updated CDAI table with “>” to prevent overlap in classification of severity; references reviewed and updated.	02.23.21	05.21
RT4: updated FDA approved indications to reflect pediatric extensions for Cyltezo in JIA and CD.	11.01.21	
2Q 2022 annual review: no significant changes; reiterated requirement against combination use with a bDMARD or JAKi from Section III to Sections I and II; updated criteria to reflect pediatric extension for UC to include patients 5 years of age and older; references reviewed and updated.	03.28.22	05.22
RT4: added biosimilars Abrilada and Hulio to policy; added new dosage form (single-dose glass vial) for Hadlima; updated FDA approved indications to reflect pediatric extensions for JIA and CD indications for Abrilada, Amjevita, Hadlima, Hulio and Hyrimoz; added limitations of use for UC per PI.	08.09.22	
RT4: added new dosage form (citrate-free 40 mg/0.4 mL PushTouch and prefilled syringe) for Hadlima.	09.07.22	

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.